REMARKS/ARGUMENTS

Claims 1–20 are pending in the captioned application.

The Examiner has rejected claim 7 under 35 U.S.C. § 112, second paragraph, as "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention". Specifically, the Examine states, "claim 7 recites the limitation 'activated acid moiety' in line 1. There is insufficient antecedent basis for this limitation in the claim."

In response, Applicant has amended claim 7 to replace the objected to recitation with "acidic reagent includes". Antecedent basis for this recitation is found in claim 1.

In view of the foregoing, Applicant respectfully asserts the Examiner's rejections cannot be sustained and should be withdrawn.

The Examiner has rejected claims 1–6, 10–13 and 15–18 under 35 U.S.C. § 102(a) as "being anticipated by Keough et al (WO 00/43792)". Specifically, the Examiner states, "Keough et al anticipates the instant invention by teaching a method of identifying a polypeptide by derivatizing the N-termini of one or more peptides with one or more acidic moieties having a pKas of less than about 2 when coupled with the

polypeptide or peptide to provide one or more derivatized analytes. This method is analyzed by mass spectrometric techniques to provide a fragmentation pattern (summary)".

The Examine continues, "the fragmentation pattern of the peptide is interpreted to sequence the polypeptide (page 7, lines 1-2). Thomas et al discloses coupling an acidic moiety reagent to the N-terminus of a cysteine-containing peptide, followed by oxidation to produce peptides containing two acidic moieties (sulfonic acids). The preferred acidic moieties are 2-sulfoacetyl, 2-sulfobenzoyl and 3-sulfopropionyl moieties (page 9, lines 1-15). These preferred acidic moieties are sulfonyls coupled to an ester moiety such as sulfosuccinic anhydride, and 2-sulfobenzoic acid cyclic anhydride and others (page 9, lines 1-30)."

The Examiner concedes, "Keough et al is silent with respect to the half-life of the acid reagent not being less than 10 minutes, however, it is the Examiner's position that this teaching is inherent to what the instant reference teaches. Keough et al teaches the acid reagents utilized in the instant invention, therefore these reagents will inherently exhibit a half-life in aqueous solution of not less than 10 minutes".

In response, Applicant respectfully disputes the Examiner's contentions, and specifically, disputes that the Keough, et al. reference teaches "sulfonyls coupled to an ester moiety". Specifically, claim 1 recites that the acidic reagent contains "a sulfonyl moiety coupled to an ester moiety", but such is neither taught nor even suggested by the Keough, et al. reference. While Applicant concedes that Keough, et al. does teach coupling of sulfonyls to anhydride reagents, these are not esters. The benefits of use of the reagents of the instant invention are disclosed at pages 8–11 of the captioned application, and include aqueous stability. Indeed, as stated at page 9, lines 5–11, one of the advantages of the instant invention compared to the disclosure of the Keough, et al. reference "resides in the fact that according to the present invention all steps can be carried out under aqueous conditions. As previously suggested technology required to dry-down steps and several small pH changes from basic to acidic, and vice versa, the present method is much more amenable to automation".

Thus, Applicant respectfully asserts that the Keough, et al. reference neither anticipates nor renders obvious the claimed invention inasmuch as it fails to teach the recited acidic reagents.

In view of the foregoing, Applicant respectfully asserts the Examiner's rejections cannot be sustained and should be withdrawn.

The Examiner has rejected claims 13–14 under 35 U.S.C. § 102(e) as "being anticipated by Little et al (USP6,322,970)". Specifically, the Examine states, "Little et al anticipates the instant reference by teaching reagents comprising a sulfonyl moiety coupled to an ester moiety and a reagent selected from the group consisting of 3-sulfopropionic N-hydroxysuccinimide esters (column 59, lines 65-67)".

In response, Applicant respectfully asserts that they cannot understand the Examiner's rejection. Specifically, the cited passage of Little, et al. discloses a linker which is suitable for attaching a peptide to a solid support in the "activated carboxy form such as sulfo-NHS ester". However, there is no disclosure, nor even any suggestion, of a reagent which can be utilized in a method of identifying a polypeptide (claim 13) or suitable for use in peptide derivatization in an aqueous solution (claim 14) as recited in the claims. Accordingly, Applicant respectfully asserts that the Examiner's rejections cannot be sustained and should be withdrawn.

The Examiner has rejected claims 7–9 and 19 under 35 U.S.C. § 103(a) as "being unpatentable over Keough et al in view of Little et al (USP#6,322,970)". Specifically, the Examiner states, "the teachings of Keough et al are set forth above and differ from the

instant claims by not disclosing a sulfonyl group being coupled to a particular ester such as N-hyroxysuccinimide (NHS) ester".

The Examiner continues, "Little et al discloses a process for determining the identity of a target polypeptide using mass spectroscopy (abstract). Little et al discloses that target polypeptides can be captured by conjugation to a solid support by immobilizing. The conjugation can be mediated through a linker such as a sulfo-N-hydroxysuccinimide (NHS) ester that facilitates conjugation of the polypeptide through it amino terminus..." The Examiner further states, "claim 12 recites a step of protecting lysine residues prior to derivatizing. Little et al discloses that the termini of a target polypeptide are more reactive than the amino acid side groups and therefore the amino acid residues should be blocked prior to performing the reaction of interest (column 60, lines 27-50)".

The Examiner concludes, "it would have been obvious to one of ordinary skill in the art to modify the reference of Keough et al to couple an N-hydroxysuccinimide (NHS) ester to a sulfonyl group taught by Little et al to facilitate conjugation of peptides to a solid support which has the advantage of being manipulated so that reagents and undesirable reaction products can be washed from the remaining immobilized

polypeptide, which can then be cleaved from the solid support and analyzed by mass spectrometry (column 60, lines 17-27)".

In response, Applicant respectfully points out that the Little, et al. reference discloses the utilization of NHS esters to facilitate attachment to a solid support. As stated at column 4, lines 38–52, this immobilization provides "a means to isolate the polypeptide, as well as a means to manipulate the isolated target polypeptide prior to mass spectrometry". Such is quite different from the instant invention wherein the derivatization is done in aqueus solution and does not require attachment to a solid support. The benefits of such aqueous solution derivatization are discussed above, and are neither disclosed nor even suggested by either the Keough, et al. or Little, et al. references.

In view of the foregoing, Applicant respectfully asserts the Examiner's rejections cannot be sustained and should be withdrawn.

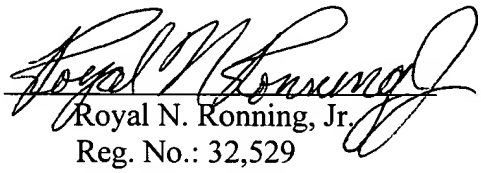
Applicant takes note of the two references made of record by the Examiner and declines to comment on such references as such references are included in a rejection.

In view of the foregoing, Applicant respectfully asserts the Examiner's rejections cannot be sustained and should be withdrawn. Applicant believes that the claims, as amended, are in allowable form and earnestly solicit the allowance of claims 1–20.

Early and favorable consideration is respectfully requested.

Respectfully submitted,

AMERSHAM BIOSCIENCES CORP

By: 
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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on August 17, 2004.

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